Identification of a subpopulation of cells with cancer stem cell properties in head and neck squamous cell carcinoma.

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Public Summary:

Scientific Abstract:
Like many epithelial tumors, head and neck squamous cell carcinoma (HNSCC) contains a heterogeneous population of cancer cells. We developed an immunodeficient mouse model to test the tumorigenic potential of different populations of cancer cells derived from primary, unmanipulated human HNSCC samples. We show that a minority population of CD44(+) cancer cells, which typically comprise <10% of the cells in a HNSCC tumor, but not the CD44(-) cancer cells, gave rise to new tumors in vivo. Immunohistochemistry revealed that the CD44(+) cancer cells have a primitive cellular morphology and costain with the basal cell marker Cytokeratin 5/14, whereas the CD44(-) cancer cells resemble differentiated squamous epithelium and express the differentiation marker Involucrin. The tumors that arose from purified CD44(+) cells reproduced the original tumor heterogeneity and could be serially passaged, thus demonstrating the two defining properties of stem cells: ability to self-renew and to differentiate. Furthermore, the tumorigenic CD44(+) cells differentially express the BMI1 gene, at both the RNA and protein levels. By immunohistochemical analysis, the CD44(+) cells in the tumor express high levels of nuclear BMI1, and are arrayed in characteristic tumor microdomains. BMI1 has been demonstrated to play a role in self-renewal in other stem cell types and to be involved in tumorigenesis. Taken together, these data demonstrate that cells within the CD44(+) population of human HNSCC possess the unique properties of cancer stem cells in functional assays for cancer stem cell self-renewal and differentiation and form unique histological microdomains that may aid in cancer diagnosis.

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